Screening For G6PD Deficiency

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Background on G6PD

- G6PD is an enzyme in the pentose phosphate pathway
- Converts NADP+ to NADPH
- G6PD deficiency is a sex-linked genetic disorders, with full expression in males
- Persons who are G6PD deficient are at increased risk for experiencing hemolytic anemia when taking primaquine

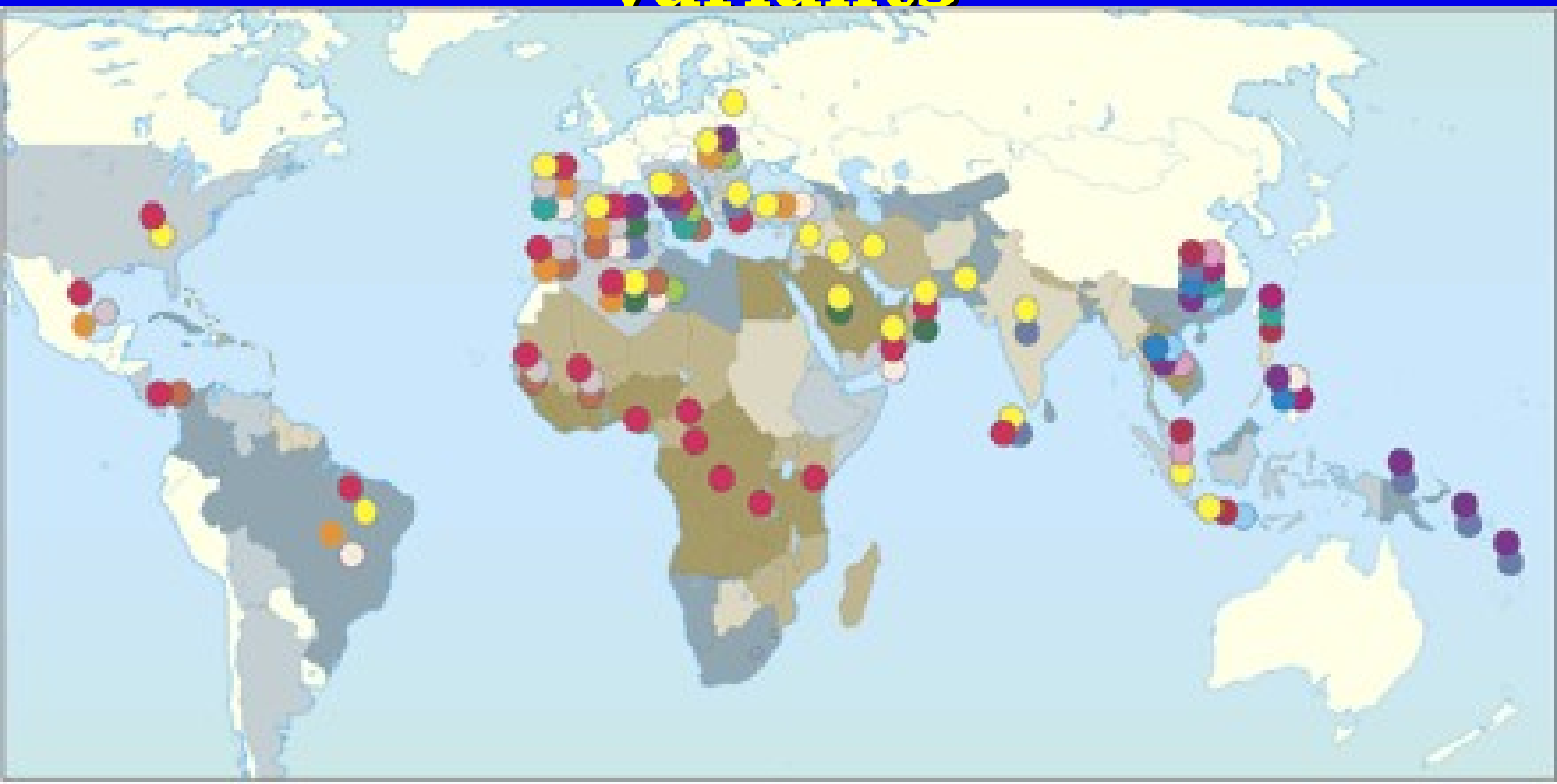
G6PD Genetic Variants

- Two most important for U.S. Army (out of 400):

- (A -) Variant affects approximately 10% of African Americans
  - enzyme usually >10% normal

- (B -) Variant (MED) is the most common type affecting people from Eastern Mediterranean
  - Enzyme usually <10% of normal

Geographic Distribution of G6PD Variants



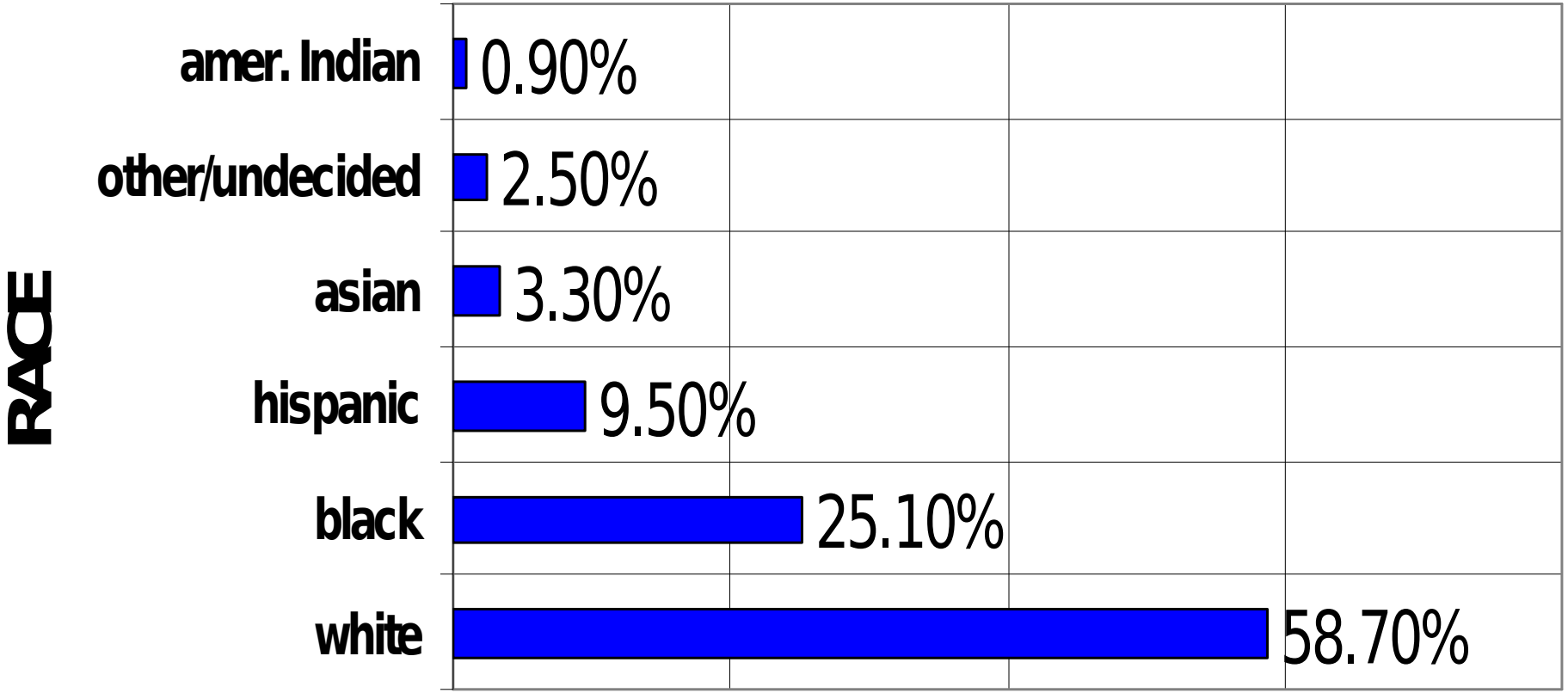
Mediterranean (B-) Variants

- Serious hemolysis can occur following one dose of 15 mg primaquine base
- Patient may require blood transfusion often hemolyzing > 50% erythrocytes
- Complications include:
  - Acute Renal Failure
  - High Output Cardiac Failure
  - Anoxia and Death

Prevalence of (B-) Variant G6PD

- The frequency of the (B-) variant differs markedly among different populations
  - < 1.0% American Caucasians
  - 2-9% of Greek
  - 0.5-1.0% of Italians
  - 3-35% of Sardinians
  - and up to 50% of Kurdish Jews

ARMY ACTIVE DUTY DEMOGRAPHIC SOLDIER POPULATION (FY 2001)



Drugs and Chemicals That Should Be Avoided by Persons With G6PD Deficiency

- Acetanilid
- Furoxone
- Methylene Blue
- Nalidixic acid
- Naphthalene
- Nitrofurantoin
- Pyridium
- Primaquine
- Sulfacetamide
- Sulfamethoxazole
- Sulfanilamide
- Sulfapyridine
- Urate Oxidase
- Phenylhydrazine

Use of Primaquine and G6PD Deficiency

- **Primaquine is the only drug available that kills liver stage parasites to prevent late malaria relapse in *Plasmodium vivax, ovale***

- **Dosing Regimens**
  - **Two regimens are used by the U.S. Army**
    - **15 mgs of primaquine base daily times 14 days**
    - **45 mgs primaquine base taken weekly for 8 weeks**

Estimates of Hemolytic Disease from Defense Medical Surveillance System

- 5 active duty soldier inpatients with glutathione related hemolytic anemia (282.2) during previous 10 years (all black, 4/5 male)
- 9 inpatients with acquired non-autoimmune hemolytic anemia (283.1) which probably includes some G6PD (8/9 male, 2/9 black)
- No ability to relate hemolysis to primaquine

AFEB 28 April 1998 Decision

- **Screen prior to deployment to *P vivax* area those soldiers who will be taking primaquine for malaria prophylaxis on redeployment**

- **Record results of G6PD testing in medical record such that it is immediately available when primaquine decision is made by medical personnel**

Current Question For AFEB

- **Should the US Army screen its soldiers for G6PD deficiency routinely as is already done by the US Navy and US Air Force?**
  - **On entry to service**
  - **Catch up program required for rest of force**
  - **Relationship to usage of primaquine**

US Navy Recruit G6PD Screening

- Overall prevalence of G6PD
- 1998 1.9% (197 / 10,158)
- 2000 2.12% (1073 / 50,513)
- 2001 2.34% (1148 / 48,975)

1998 US Navy G6PD Data by Race

- Caucasian 0.4% (24/5770)
- African American 7.6% (144/1903)
- Hispanic 0.9% (10/1140)
- Native/Alaskan 0.0% (0/398)
- Asian 1.8% (7/373)

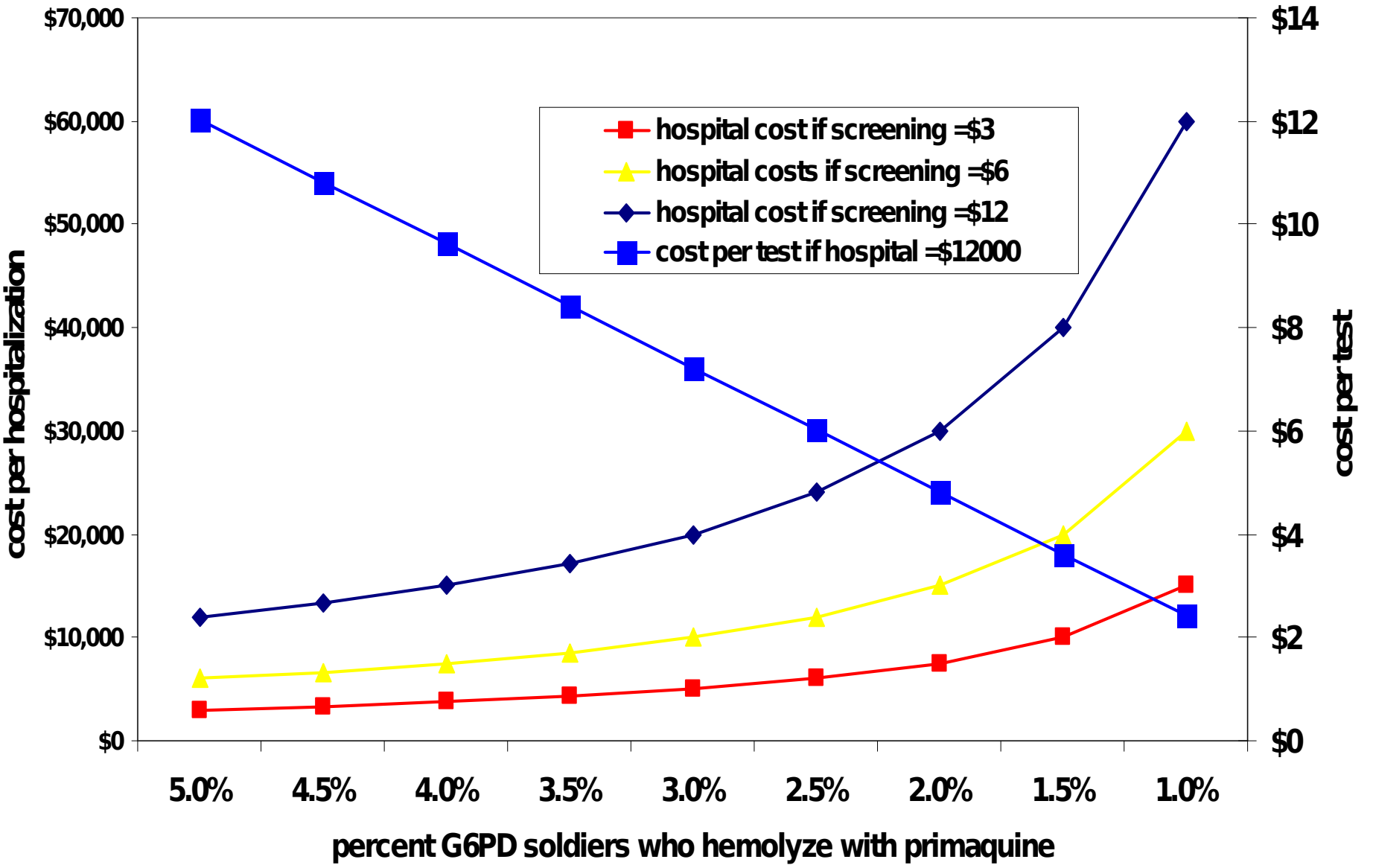
G6PD Status in USAF Recruits from July 2002-March

Month	# Tested	Deficient Number	Deficient Percent
July	994	16	1.61%
August	3517	63	1.79%
September	3521	42	1.19%
October	4097	78	1.90%
November	2976	83	2.79%
December	3018	52	1.72%
January	4532	78	1.72%
February	3511	80	2.28%
March	2792	47	1.68%
Total	**28958**	**539**	**1.86%**

Costs of G6PD Screening vs. Not Screening

- Cost to screen one soldier varied from $3 at USAF basic training site to $26 if ordered from commercial lab
- Cost of mild hemolysis cases or few primaquine break-through vivax cases are ignored
- Hospitalization costs $12,040 (1998) was best estimate for major hemolytic event requiring hemodialysis / blood transfusion
- Key question is “What percent of men who are G6PD deficient will have hemolysis severe

Cost Equivalency Points for G6PD Screening



Brigade to Receive Post-deployment Primaquine

- For a 10,0000 person cohort in a malarious area
  - Assuming $10 per person to screen
  - Assuming 2% of total is G6PD deficient
  - Hospitalization cost of severe hemolytic event is $10,000

- Break even point on costs is if 5% of those deficient have severe hemolysis on receiving primaquine or an overall hemolysis rate of 1 per 1000 soldiers

Rare Serious Event Risk Management

- If relatively few persons receive primaquine, then screening on entry is not cost-effective
- If large number of soldiers are stationed in Iraq, then one can expect some severe reactions following terminal primaquine treatment
- Bad publicity and legal costs resulting from a single G6PD hemolysis case with bad outcome

Issues for Consideration

- Does risk of severe hemolytic event out weigh cost of screening program?
- Can G6PD screening information actually inform decision to use primaquine? Accurate and available information?
- If recruits are to be screened, how urgently should rest of force also be screened?

Questions?